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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Sandal et al.

Serial No.: 09/426,340 Group Art Unit: 1655

Filed: October 25, 1999 Examiner: Johannsen, D.

For: Method For Generating A Gene Library

AMENDMENT AND REMARKS

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

In response to the Office Action issued 16 June 2000, please cancel claims 20 and 26, and amend the remaining claims as follows:

1. (Amended) A method for generating a gene library from an environmental pool of organisms isolated from soil, animal dung, insect dung, insect gut, animal stomach, sea or lake water, waste water, sludge, or sediment, which gene library is enriched in DNA encoding a polypeptide with an activity of interest, which method comprises:

a) subjecting the environmental pool of organisms to cultivation [in a medium and/or] under conditions [suitable for enriching said] wherein the pool of organisms is enriched in organisms harbouring said DNA; and

b) preparing a gene library from the [resulting] enriched pool of organisms.

2. (Amended) The method [according to] of claim 1, wherein the conditions are culturing in a medium contains a substrate for the gene product encoded by said DNA.

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3. (Amended) The method [according to] of claim 2, wherein the substrate constitutes the carbon source and/or nitrogen source of the medium.

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4. (Twice Amended) The method [according to] of claim 2, wherein the substrate comprises pectin, amylose, cellulose, galactose, xylose or arabinose or a combination thereof.

B3

5. (Amended) The method [according to] of claim 1, wherein the [enrichment is achieved] pool of organisms is enriched by one or more growth restrictions.

6. (Amended) The method [according to] of claim 5, wherein the growth [conditions] restrictions comprise pH and temperature.

B4

7. (Twice Amended) The method [according to] of claim [1] 5, wherein the growth [conditions] restrictions [of step a) used for achieving the enrichment] are pH 9-11 and temperature 50-70°C.

8. (Amended) The method [according to] of claim 1, wherein the environmental pool of organisms is isolated from an animal stomach or an insect gut.

9. (Amended) The method [according to] of claim 8, wherein the pool of [micro]organisms is isolated from a cow's rumen.

B5

10. (Amended) The method [according to] of claim 8, wherein the pool of [micro]organisms is isolated from the gut of an insect of the [Isoptera] *Isoptera*, [Lepidoptera] *Lepidoptera*, [Coleoptera] *Coleoptera*, or [Diptera] *Diptera* families.

11. (Amended) The method [according to] of claim 10, wherein the pool of [micro]organisms is isolated from the gut of insects selected from the group consisting of [Agrotis, Neotermes castaneus, Tineola bisselliella, and Melolontha vulgaris] *Agrotis, Neotermes castaneus, Tineola bisselliella*, and *Melolontha vulgaris*.

B4

12. (Twice Amended) The method of claim 8, wherein prior to isolation, the pool of [micro]organisms is enriched by supplying feed to the animal or insect, which comprises a substrate for the polypeptide with an activity of interest.

sub D2

13. (Amended) The method [according to] of claim 1, wherein the gene [libraries are] library is riched in DNA encoding an enzyme [activity] of interest.

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14. (Amended) The method [according to] of claim 13, wherein the enzyme of interest comprises a hydrolase, an oxidoreductase, a transferase, a lyase or a ligase.

15. (Amended) The method [according to] of claim 14, wherein the enzyme of interest comprises a protease, lipase, beta-galactosidase, lactase, polygalacturonase, beta-glucoamylase, esterase, hemicellulase, peroxidase, oxidase, laccase or glucose oxidase.

16. (Amended) The method [according to] of claim 14, wherein the enzyme of interest is a pectinase, an amylase, [an] a galactanase, an arabinase, a xylanase, or a cellulase.

17. (Reiterated) The method of claim 1, wherein the environmental pool of organisms comprises microorganisms.

18. (Reiterated) The method of claim 17, wherein the environmental pool of organisms comprises enzyme producing microorganisms.

B8

19. (Amended) The method of claim 17, wherein the microorganisms comprise [Eubacteria] *Eubacteria*, [Archaebacteria] *Archaebacteria*, fungi, algae and/or protozoa.

B9

21. (Amended) A method of selecting a DNA sequence encoding a polypeptide of interest from an environmental pool of organisms isolated from soil, animal dung, insect dung, insect gut, animal stomach, sea or lake water, waste water, sludge, or sediment, which method comprises:

sub D3

a) subjecting the environmental pool of organisms to cultivation [in a medium and/or] under conditions [suitable for enriching said] wherein the pool of organisms is enriched in organisms harbouring said DNA; [and]

b) producing gene libraries from the [resulting] enriched pool of organisms;

c) screening the libraries of step b) for DNA containing the desired gene; and

d) selecting the DNA sequence of interest resulting from the screening of step c).

22. (Amended) A method [according to] of claim 21, wherein the [gene library comprises an enzyme-producing gene of interest] desired gene encodes an enzyme .

B9 Concl'd Sub D4

23. (Amended) The method of claim 21, wherein the gene [library is screened for enzymes under conditions which the enzyme is active] libraries are screened in step c) for an active enzyme.

24. (Amended) The method of claim 21, wherein the [gene libraries are screened for] desired gene encodes one of a pectinase, amylase, galactanase, arabinase, xylanase or cellulase.

25. (Amended) A gene library prepared from an [enriched] environmental pool of organisms enriched in DNA encoding a polypeptide with an activity of interest by the method of claim 1.

B10 Sub D5

27. (Amended) The gene library [according to claim 26] of claim 25, wherein the DNA is an enzyme which comprises a pectinase, an amylase, [an] a galactanase, an arabinase, a xylanase or a cellulase.

REMARKS

Claims 20 and 26 are cancelled. Therefore claims 1-19, 21-25, and 27 are pending. The claims are amended in response to the Examiner's comments under the second paragraph of section 112. No new matter is added by this amendment, and the Examiner is respectfully requested to enter the amendment. Reconsideration of the claims in view of the above amendments and following remarks is respectfully requested.

I. Formal Matters

Claims 16 and 26-27 were objected to for grammar. Claim 26 is cancelled. Accordingly, claims 16 and 27 are corrected by amendment above. This objection may now be withdrawn.

II. Rejections Under 35 USC § 112, second paragraph.

A. Claims 1-27 were rejected as indefinite for recitation of the terms "environmental pool of organisms" and "enriched environmental pool of organisms." In response, claims 1 and 21 are amended to add the limitation of environmental pool of organisms to those "isolated from soil, animal dung, insect dung, insect gut, animal stomach, sea or lake water, waste water, sludge, or sediment". Accordingly, it is believed that this rejection may now be withdrawn.

B. Claims 1-24 were rejected as indefinite for recitation of the phrase "subjecting the environmental pool of organisms to cultivation in a medium and/or under conditions **suitable for enriching said pool of organisms** harbouring said DNA." In response, claims 1 and 21 are amended such that step a) reads: "subjecting the environmental pool of organisms to cultivation under conditions wherein the pool of organisms is enriched in organisms harbouring said DNA". Accordingly, it is believed that this rejection may now be withdrawn.

C. Claims 1-24 were rejected as indefinite for recitation of a "resulting" enriched pool of organisms. Accordingly, the word "resulting" is deleted from claims 1 and 21.

D. Claims 2-4 were rejected as indefinite. It is believed that this rejection is rendered moot by amendments to claim 1.

E. Claims 5-6 were rejected as indefinite for recitation of the phrase "the enrichment." Claim 5 is amended to correct the language of the claim, and it is believed that the rejection may now be withdrawn.

F. Claims 6 and 7 were rejected as indefinite for recitation of the limitation "the growth conditions." Claims 6 and 7 are corrected by changing the word "conditions" to "limitations" consistent with the recitation in claim 5. Accordingly, this rejection may now be withdrawn.

G. Claims 9-12 were rejected as indefinite for lack of antecedent basis for the phrase "the pool of microorganism." Claims 9-12 were amended to remove "micro" from each recitation. Accordingly, it is believed this rejection may now be withdrawn.

H. Claim 12 was rejected as indefinite. Claim 12 is amended to clarify that the enrichment is achieved prior to isolation of the environmental pool of organisms.

I. Claims 13-16 and 14-16 were rejected for reciting limitations without sufficient antecedent basis. Claim 13 was amended to change "libraries" to "library" and to remove the word "activity." Accordingly, it is believed that proper antecedent basis is established for the recited terms.

J. Claim 20 was rejected for recitation of the term "said organisms." This rejection is rendered moot by cancellation of claim 20.

K. Claims 21-24 were held to be indefinite for recitation of the phrase "method of selecting a DNA sequence of interest." In response, claim 21 is amended to recite "A method of selecting a DNA sequence encoding a polypeptide of interest from an environmental pool of organisms isolated from soil, animal dung, insect dung, insect gut, animal stomach, sea or lake water, waste water, sludge, or sediment, which method comprises: a) subjecting the environmental pool of organisms to cultivation under conditions wherein the pool of organisms is enriched in organisms harbouring said DNA; and b) producing gene libraries from the enriched pool of organisms; c) screening the libraries of step b) for DNA containing the desired gene; and d) selecting the DNA sequence of interest resulting from the screening of step c). In light of these amendments, it is believed this rejection may now be withdrawn.

L. Claims 22-23 were rejected as indefinite for insufficient antecedent basis for the recitation of "gene library." The rejected claims are amended in response, and it is believed that the amended claims overcome this rejection.

M. Claim 23 was rejected for indefiniteness in how it limits claims 21. Claim 23 is amended to limit the screening step recited in claim 21 as a screening "for an active enzyme." Accordingly, it is believed this rejection may now be withdrawn.

N. Claim 23 was further rejected for recitation of "the enzyme." Claim 23 is corrected.

O. Claim 24 was rejected as indefinite in how it intends to further limit claim 21. Claim 24 is amended to define the desired gene.

P. Claims 25-27 were rejected as indefinite. Claim 26 is cancelled. In response, claim 25 is amended to recite "A gene library prepared from an environmental pool of organisms enriched in DNA encoding a polypeptide with an activity of interest by the method of claim 1. In light of this amendment, it is believed that this rejection may now be withdrawn.

Q. Claims 26-27 were rejected as indefinite. Claim 26 is cancelled, and claim 27 amended to depend on claim 25. Accordingly, it is believed that this rejection may now be withdrawn.

III. Rejections Under § 102(b).

Claims 1-3, 5-6, 13-15, 17-23, and 25-26 were rejected as anticipated by Duvick et al. (WO 96/06175). This rejection is respectfully traversed.

Under the standard required for anticipation under § 102(b), the cited prior art reference is required to disclose every element of the claimed invention. A reference that merely contains substantially the same elements is insufficient to "anticipate" the claimed invention. Jamesbury Corp. v. Litton Industrial Products, Inc., 225 USPQ 253 (Fed. Cir. 1985). Similarly, a reference that only broadly teaches the invention is also considered insufficient to establish anticipation. Kalman v. Kimberly-Clark Corp., 218 USPQ 781 (Fed. Cir. 1983).

The invention as claimed. Amended claim 1 is drawn to a method for generating a gene library from an environmental pool of organisms isolated from soil, animal dung, insect dung, insect gut, animal stomach, sea or lake water, waste water, sludge, or sediment, which gene library is enriched in DNA encoding a polypeptide with an activity of interest, which method comprises: a) subjecting the environmental pool of organisms to cultivation under conditions wherein the pool of organisms is enriched in organisms harbouring said DNA; and b) preparing a gene library from the enriched pool of organisms.

The Duvick et al. reference (WO 96/06175). Duvick et al. describes a method for isolating organisms from plant material and culturing under conditions where organisms expressing a desired characteristic are selected. Genomic libraries are prepared from the selected organisms.

The analysis under § 102(b). In contrast to the instant claimed invention, which utilizes a method in which (1) an environmental pool of organisms is enriched by growing the pool on a substrate for the sought activity and (2) making a multi-organism gene library for the enriched pool directly, which is then (3) expressed in a host cell, allowing for (4) selection for gene encoding the activity of interest, Duvick et al. teaches the following: (1) enriching a pool or organisms from an agricultural crop by growing the pool on a substrate (fumonisin, FB1 or FB2), (2) isolating positive organisms through several rounds of selection, (3) making a gene library from a selected organism, (4) cloning and expressing the library in a host cell, (5) selecting a positive clone, and (6) isolating the gene encoding the sought for activity.

As the above comparison shows, the instant invention avoids several time and labor intensive steps because the instant invention is not concerned with the source of the gene encoding the activity of interest, and thus does not entail isolation of a strain.

Accordingly, Applicants submit that the Examiner has failed to establish a *prima facie* case of anticipation, and this rejection should be withdrawn.

IV. Rejections Under § 103(a).

A. Claims 4, 7, 16, 24, and 27 were rejected as obvious over Duvick et al. (WO 96/06175) in view of Sarkar and Upadhyay (Folia Microbiologica (1993) 38:29-32). This rejection is respectfully traversed.

The above remarks under § 102 are fully applicable to this rejection and are herein specifically incorporated by reference. Duvick et al. teaches a method which requires extensive strain selection and screening. Duvick et al. is absent a realization that these time consuming, labor intensive steps may be avoided. The secondary reference does not cure the defects of Duvick et al. The Examiner describes that "Sarkar and Upadhyay disclose that *Bacillus htermoalcaliphilus* isolated from an environmental sample . . ." As the above analysis points out, the instant invention does not either go through the isolation/selection steps taught by Duvick et al., or starts through the isolation of an organism. Accordingly, it is believed that the Examiner has failed to establish a *prima facie* case of obviousness, and that this rejection should thus be withdrawn.

B. Claims 4, 8-9, 16, 24, and 27 were rejected as obvious over Duvick et al. (WO 96/06175) in view of Cotta (Appl. Environment. Microbiol. (1988) 54:772-776). This rejection is respectfully traversed.

The above remarks are fully applicable to this rejection and are herein specifically incorporated by reference. The addition of Cotta fails to cure the defects of Duvick et al. Knowledge that there are several bacteria in the presence of the rumen of cattle fails to provide instructions as to which of Duvick et al. selection/isolation/screening steps could be dispensed with. Accordingly, it is believed that the Examiner has failed to establish a *prima facie* case of obviousness, and that this rejection should thus be withdrawn.

C. Claims 4, 8, 10, 12, 16, 24, and 27 were rejected as obvious over Duvick et al. (WO 96/06175) in view of Jacobsen and Schlein (J. Euk. Microbiol. (1997) 44:216-219). This rejection is respectfully traversed.

The above remarks are fully applicable to this rejection and are herein specifically incorporated by reference. The addition of Jacobsen et al. fails to cure the defects of Duvick et al. Knowledge that "*Leishmania* present in the midgut of the sandfly *phlebotomus papatasi* produce celllulases" fails to provide instructions as to which of Duvick et al. selection/isolation/screening steps could be dispensed with. Accordingly, it is believed that the Examiner has failed to establish a *prima facie* case of obviousness, and that this rejection should thus be withdrawn.

D. Claim 11 is rejected as obvious over Duvick et al. (WO 96/06175) in view of Jacobsen and Schlein (J. Euk. Microbiol. (1997) 44:216-219), and further in view of Siegle et al. (US 4,027,037). This rejection is respectfully traversed.

The above remarks are fully applicable to this rejection and are herein specifically incorporated by reference. The addition of Jacobsen et al. and Siegle et al. fails to cure the defects of Duvick et al. Knowledge that "*Leishmania* present in the midgut of the sandfly *phlebotomus papatasi* produce celllulases" of Jacobsen et al. combined with "a variety of orders and species of arthropods" of Siegle et al. fails to provide instructions as to which of Duvick et al. selection/isolation/screening steps could be dispensed with. Accordingly, it is believed that the Examiner has failed to establish a *prima facie* case of obviousness, and that this rejection should thus be withdrawn.

Conclusion

Applicants submit that in light of the above amendments and remarks, the application is in condition for allowance, which action is respectfully requested.

Respectfully submitted,

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